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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,452	02/25/2002	Stefan Anker	101195-65	1403

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NORRIS, MCLAUGHLIN & MARCUS, P.A.
875 THIRD AVE
18TH FLOOR
NEW YORK, NY 10022

EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,452	ANKER ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,20-22 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 4, 20-22 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/30/06 has been entered.

Claims 1, 3, 4, 20-22 and 24 are pending

2. *Claims 1, 3, 4 20-22 and 24, drawn to a method of treating and ameliorating endotoxin-mediated cachexia are under consideration in the instant application.*

3. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in United Kingdom on 03/09/1999 . It is noted, however, that applicant has not filed a certified copy of the 9905315.9; 9905300.1; 9905310.0;9905307.6;9905314.2 applications as required by 35 U.S.C. 119(b).

The rejection of claims 1-6 and 19-20 under 35 U.S.C. 102(b) as being anticipated by US Patent 5639744 as evidenced by US Patent 4377595 and/or US Patent 4,898,879 and under 35 U.S.C. 102(e) as being anticipated by US Patent 6251,884 or US Patent 5,869,265 as evidenced by US Patent 4377595 and/or US Patent 4,898,879 is hereby withdrawn in view of the amendment to claim 1. However, this rejection will be re-introduced when the **new matter** (*a method of treating and ameliorating endotoxin-mediated cachexia in a human patient*) is deleted from amended claim 1

In view of the amendment, filed 05/30/06 the following rejections remain:

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 3, 4, 20-22 and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting the LPS-stimulated cytokine

production in patients with cachexia, comprising administration of UDCA, does not reasonably provide enablement for a method of treating and ameliorating endotoxin-mediated cachexia in human patient comprising administering UDCA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim for the same reasons set forth in the previous Office Action mailed on 03/23/05.

Applicants argument filed on 05/30/06 have been fully considered, but have not been found convincing.

Applicant asserts that: (i) amended claim 1 now directed to a method of treating and ameliorating endotoxin mediated cachexia; (ii) Exhibit 1 submitted by Dr. Anker in the Declaration under 37 C.F.R.1.132, shows an experiment conducted in human patients treating patients with cachexia.

Contrary to Applicant's assertion as has been stated in the previous Office Action, the specification only discloses detailed *in vitro and in vivo* data that administration of UDCA can inhibit the LPS-stimulated cytokine production in whole blood of patients with cachexia. The specification does not adequately teach how to effectively treat and ameliorate endotoxin-mediated cachexia in human patient by administering to said patient an effective amount UDCA. Moreover, no animals models were used to study the effectively of treating or ameliorating endotoxin-mediated cachexia in a patient comprising administering an effective amount of UDCA. Since there is no animal model studies and data in the specification to show the effectively the effectively of treating or ameliorating endotoxin-mediated cachexia in a human patient comprising administering an effective amount of UDCA it is unpredictable how to correlate limited *in vitro* results with *in vivo* use. The specification does not provide sufficient teaching as to how it can be assessed that treating or ameliorating or ameliorating endotoxin-mediated cachexia in a human patient was achieved after the administration of a therapeutically effective amount of UDCA. Trauner et al., (IDS) teach that UDCA is of unproven efficacy in non-cholestatic disorders, including liver diseases (see entire document, Abstract in particular). Moreover, Applicant acknowledges that the effects of UDCA are conflicting (see page 5 of the Specification as filed). Demonstrating *in vitro and in vivo* that administration of UDCA can inhibit the LPS-stimulated cytokine production in the whole blood of patients with cachexia cannot alone support the predictability of a method of treating and ameliorating endotoxin-mediated cachexia in a human patient by administration to the subject an effective amount of UDCA.

With regards to Applicant statement that " Exhibit 1 submitted in the Declaration under 37 C.F.R.1.132, shows an experiment conducted in human patients treating patients with cachexia."

It is noted that there is no Exhibit 1 in the Declaration under 37 C.F.R.1.132 submitted by Dr. Anker on 05/30/06.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed a method of treating or ameliorating endotoxin-mediated cachexia in a human patient by administration to the subject an effective amount of UDCA in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

6. Also an issue is that Claims 1, 3, 4, 20-22 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection**.

"human patient" claimed in claims 1 represent a departure from the specification and the claims as originally filed. The specification and the claims as originally field only support the general term "patient".

Applicants argument filed on 05/30/06 have been fully considered, but have not been found convincing.

Applicant asserts tat it would be obvious to one skilled in the art that the term "patient" can mean "human patient".

Contrary to Applicant's assertion obviousness is not the standard for the addition of new limitations to the disclosure as filed. It is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977). New Matter is a written description issue.

7. Claims 1, 3, 4, 20-22 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,251,884 or US Patent 5,869,265 or US Patent 5639744 each in view of US Patent 4377595 and/or US Patent 4,898,879 and newly cited US Patent 5,087453 for the same reasons set forth in the previous Office Action mailed on 03/23/05.

Applicants argument filed on 05/30/06 have been fully considered, but have not been found convincing.

Applicant asserts that: (i) none of references describing a method of treating and ameliorating endotoxin-mediated cachexia comprising administering to the patient an effective amount of UDCA; (ii) none of the references disclosed human patients and only disclosed rat data.

Applicants have traversed the primary and the secondary references pointing to the differences between the claims and the disclosure in each reference. Applicant is respectfully reminded that the rejection is under 35 USC103 and that unobviousness cannot be established by attacking the references individually when the rejection is based on the combination of the references. see In re Keller, 642 F.2d 4B, 208 USPQ 871, 882 (CCPA 1981) See MPEP 2145. This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968).

With regards to Applicant's comments that none of the references disclosed human patients. It is noted that all cited references disclosed the general genus of "patient". One skill in the art would immediately recognized that there are only two species in that genus: only veterinarians and physicians have patients. When the reference teaches a small genus which places a claimed species in the possession of the public as in *In re Schaumann,* 572 F.2d 312, 197 USPQ 5 (CCPA 1978), and the species would have been obvious even if the genus were not sufficiently small to justify a rejection under 35 U.S.C. 102. See MPEP § § 2131.02 and 2144.08 for more information on anticipation and obviousness of species by a disclosure of a genus.

With regards to Applicant's comments that US Patent '744 only disclosed rat data. It has been previously settled that " even if a reference discloses an inoperative devise, it is prior art for all it teaches" *Beckman Instruments v LKB Produkter* AB, 892 F.2d 1547,1551, 13 USPQ2d 1301,1304 9Fed. Cir.1989). See MPEP 2121.01.

US Patent '884 teaches a method of treating liver diseases, including liver cirrhosis, comprising administering to a patient an effective amount of UDCA (see entire document, Abstract and column 2 in particular). US Patent '884 teaches various ways of administering UDCA, including orally and intravenously administration (see column 4 ,8 and 13 in particular).

US Patent '265 teaches a method of treating liver diseases, including liver cirrhosis, comprising administering to a patient an effective amount of UDCA (see entire document, Abstract and column 35 and Example IX in particular).

US Patent '744 teaches a method of treating liver diseases, including liver cirrhosis, comprising administering to a patient an effective amount of UDCA (see entire document, Abstract and column 3 in particular).

The claimed invention differs from the reference teaching in that the US Patent ' 884 or US Patent ' 265 or US Patent ' 744 does not teach a method of treating and ameliorating endotoxin mediated cachexia, comprising administrating an effective amount of UDCA .

US Patent'595 teaches that the diseases such as cirrhosis of the liver results in a body wasting or cachexia (see column 3 in particular).

US Patent '879' teaches that liver diseases such as cirrhosis of the liver results in a significant body wasting or cachexia and that restoring liver function would be beneficial for the patient with weight loss (see column 4 in particular).

US Patent '453 teaches that cachexia may result from diverse causes, including heart failure , inflammatory diseases and lung disease (see entire document, column 1, lines 10-40 in particular). US Patent '453 teaches that endotoxin-mediated cachexia has been used to create a model for study of cachexia (see columns 1, 3 and 6 in particular). US Patent '453 teaches that effective method of treating cachexia would be useful in treating cachexia of various etiologies, including heart failure , inflammatory diseases and lung disease (see column 3 in particular).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of US Patent'595 or US Patent '879 and US Patent '453 to those of US Patent ' 884 or US Patent ' 265 or US Patent ' 744 to obtain a claimed method of treating and ameliorating endotoxin mediated cachexia, comprising administrating an effective amount of UDCA.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because there is a direct correlation between liver diseases such as cirrhosis of the liver and body wasting or cachexia and treating cirrhosis of the liver would be beneficial for the patient with cachexia as taught by US Patent'595 and US Patent '879 . Moreover, endotoxin-mediated cachexia is a useful model of treating cachexia and effective method of treating cachexia would be useful in treating cachexia of various etiologies, including heart failure , inflammatory diseases and lung disease as taught by US Patent '453. Treating cirrhosis of the liver can be done by administering to a patient an effective amount of UDCA are taught by US Patent ' 884 or US Patent ' 265 or US Patent ' 744 . The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144.

Claims 4 is included because the claimed functional limitation would be an obvious properties of the referenced method of treating liver cirrhosis comprising administering of UDCA. It is clear that both the prior art and claimed method administer the same compound, i.e. UDCA to the same patient, i.e. a patient with cachexia to achieve the same results. Since the reference method administering the same compound as claimed , it would be obvious that UDCA would be able to reduce the production, absorption and/or the effect of an endotoxin or reduce the available endotoxin in the patient as claimed. When the prior art method is the same as a method described in the specification, it can be assumed the method will obviously perform the claimed process absent a showing of unobvious property.

Claim 22 is included because it would be conventional and within the skill of the art to determine the optimum routes of UCDA administration . Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum routes of administration involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

The following new ground of rejection are necessitated by the amendment filed 05/30/06

8. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 24 is indefinite and ambiguous in the recitation of " wherein cachexia is due to renal failure, heart failure, rheumatoid arthritis, chronic obstructive pulmonary disease or diabetes". It is noted that preamble of the base claim 1, recited "A method of treating endotoxin-mediated cachexia". It is unclear how cachexia that is due to renal failure, heart failure, rheumatoid arthritis, chronic obstructive pulmonary disease or diabetes is endotoxin-mediated cachexia ?

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1, 3, 4 20-22 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection**.

" a method of treating and ameliorating endotoxin mediated cachexia" claimed in claim 1 represent a departure from the specification and the claims as originally filed. The passages point by the Applicant do not provide a clear support for " a method of treating and ameliorating endotoxin mediated cachexia", claimed in claim 1.

The specification and the claims as originally field only support " A method of treating or ameliorating cachexia in a patient with liver cirrhosis, renal failure, heart failure, rheumatoid arthritis, chronic obstructive pulmonary disease or diabetes".

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 571/273-8300

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MICHAIL BELYAVSKYI, PH.D.
PATENT EXAMINER
7/21/06